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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/981,310	12/16/1997	ULF LANDEGREN	1209-121P	7960

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EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/981,310	LANDEGREN, ULF	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *26 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,5,6 and 8-10* is/are allowed.

6)☒ Claim(s) *3-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6, 8-10 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Allowable Subject Matter

1. Claims 1-2, 5-6, 8-10 define over the prior art of record and are therefore allowed.

Rejections Withdrawn

2. Claim 2 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, has been obviated through deletion of the phrase "and the macromolecule is a specific antigen".

Rejections Maintained

3. Claims 3-4 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, is maintained for reasons of record in the Office Action dated July 11, 2003.

4. Claims 3 and 4 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reciting affinity reagents that are "lectins, receptors, cofactors or nucleic acids" and broaden the scope of claim 1 from which they depend because:

a. Lectins do not bind to protein macromolecules, but to carbohydrates;

b. The receptors are not defined to be protein macromolecule receptors; and

c. The nucleic acids bind to nucleic acids not proteins.

While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Response to Arguments

5. The rejection of claims 3-4 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is traversed on the grounds that "The examiner interprets claim 1 as requiring that the affinity reagents bind to protein determinants, i.e. amino acids, because the target macromolecule is a protein, and asserts that "a lectin affinity reagent may bind to the protein macromolecule via the sugar moieties on the protein."

6. It is the position of the examiner that the protein of claim 1 is not so defined to comprise the critical structural characteristics that Applicant asserts are present in order for a combination of three lectins to bind to the protein macromolecule. In order to permit a signal to be generated by nucleic acid amplification, as the claim requires, the second and third affinity reagent lectins must be bound on the macromolecule in close proximity to each other in order to generate a signal. No combination of any two lectins, of any carbohydrate binding specificity have been disclosed and enabled to permit two lectins bind to any type of protein at any two positions in order to generate a signal.

Prokaryote produced proteins are generally understood not to be glycosylated, prokaryote recombinantly produced eukaryotic proteins also would not be glycosylated, and no postranslationally modified proteins that evidence a combination of three carbohydrate epitopes in proximity to one another have not been disclosed, enabled through description, nor exemplified in the instant specification to enable any combination of three lectins to detect any protein macromolecule. The binding specificity of the lectins is not set forth in the claims, nor in

the specification so to enable a kit to detect the claimed genus of proteins with any three lectins of any carbohydrate binding specificity, with the recited functional characteristics. The person of skill in the art would denovo have to identify which of the many proteins that are known, would present lectin epitopes in a configuration to permit the recited functional characteristics.

Additionally, with respect to the meaning of the term "protein" the examiner consulted two medical dictionaries for the art recognized definition

Stedman's medical dictionary defines the term **protein** to mean*:* Macromolecules consisting of long sequences of α-amino acids [H_2N–CHR–COOH] in peptide (amide) linkage (elimination of H_2O between the α-NH_2 and α-COOH of successive residues). Protein is three-fourths of the dry weight of most cell matter and is involved in structures, hormones, enzymes, muscle contraction, immunologic response, and essential life functions. The amino acids involved are generally the 20 α-amino acids (glycine, l-alanine, etc.) recognized by the genetic code. Cross-links yielding globular forms of protein are often effected through the –SH groups of two l-cysteinyl residues, as well as by noncovalent forces (hydrogen bonds, lipophilic attractions, etc.). Therefore the term "protein" is understood to be a long sequence of amino acids.

The ***On-Line Medical Dictionary*** defines the term "protein" to be: a molecules which contain carbon, hydrogen, oxygen, nitrogen and usually sulphur, the characteristic element being nitrogen and which are widely distributed in plants and animals. (18 Nov 1997) Based upon the definition of "protein" provided by the On-Line Medical Dictionary, lectins would not serve to bind to amino acids (carbon, hydrogen, oxygen, nitrogen) or sulphur, and therefore would not function as an affinity reagent for protein macromolecules that are understood to be amino acid containing macromolecules.

Arguments directed to a critical characteristic not disclosed, taught or suggested in the instant specification sets forth a combination of arguments that are not commensurate in scope with the instantly claimed invention. No combination of three lectins has been enabled that bind

to any protein in proximity of each other to permit the conjugated oligonucleotides to undergo amplification. This is also true for cofactors, receptors and nucleic acids with respect to detecting any protein macromolecule.

7. Applicant asserts that "there are known instances of proteins that bind to nucleic acids" and implies that the claim is enabled for the combination of three nucleic acids that will bind to a single protein in proximity to one another to generate a signal.

8. The examiner did not find enabling disclosure of a combination of three nucleic acids that will all simultaneously bind to a single protein in proximity to each other. While specific species of nucleic acid binding protein my bind to a single nucleic acid, no combinations of three nucleic acids that will simultaneously bind to a single protein molecule at three different locations on the protein, two of which are in proximity to each other to generate a signal has been enabled by the instant specification.

What is claimed is not a kit with three individual reagents, two of which are conjugated with oligonucleic acids that are conjugateable to each other, but to a combination of reagents that all must bind to the same protein macromolecule simultaneously, and two of the three reagents must bind in close proximity to each other to allow the conjugatable oligonucleotides to generate an amplification signal.

Applicant through traversal seeks to define the invention to be directed to individual reagents that need not act in concert with the other two reagents. Applicant's arguments are not commensurate in scope with the instantly claimed invention that must evidence the recited

combination of functional characteristics. The enablement rejection is maintained for reasons of record and responses set forth herein.

9. The rejection of claims 3 and 4 under 35 U.S.C. 112, second paragraph, as being indefinite for reciting affinity reagents that are "lectins, receptors, cofactors or nucleic acids" and broaden the scope of claim 1 from which they depend because lectins do not bind to protein macromolecules, but to carbohydrates; the receptors are not defined to be protein macromolecule receptors; and nucleic acids bind to nucleic acids not proteins, respectively, is traversed on the grounds that:

d. Lectins bind to proteins through the sugar moieties that are present on many proteins;

e. there are many instances of nucleic acid/protein binding; and

f. the receptors of claim 3 are the affinity reagents, not the macromolecule.

10. It is the position of the examiner that the critical structural characteristics of sugar moieties is not set forth in the claims. The carbohydrate binding specificity of the lectins is not so defined to bind amino acids, the art recognized meaning of the recitation of the term "protein" per the definitions provided above (Stedman's Medical Dictionary and On Line Medical Dictionary).

With respect to "many instances of nucleic/acid/protein binding", it is the position of the examiner that the protein macromolecules recited in the claims have not been so structurally defined to be nucleic acid binding proteins. What is now claimed is a kit that will detect any protein with any three nucleic acids. Even if a protein binding protein could be detected with

one of the nucleic acid binding reagents, the other two reagents must also bind to the same protein and two of the three reagents must bind in close proximity to one another. Claim 3 is broader than that of claim 1 which requires the combination of three affinity reagents to function in concert with each other, and Applicant's arguments do not address this critical functional limitation, but asserts that proteins that bind nucleic acids are known, but does not address the fact that all three nucleic acids must bind to a single protein. Thus the traversal provides support for the examiner's position that the dependent claim is not further limiting of the independent claims as the kits of claim 3 recite nucleic acids is broader in scope than that of the independent claim, as the three nucleic acids would not bind to the same protein simultaneously as the protein has not been defined to bind three nucleic acids in the active site at the same time.

Additionally, what protein will bind to three receptors simultaneously has not been defined in the instant specification, and the binding specificity of the receptors has not been defined to be directed to any and all protein macromolecules.

In summary, while the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 8:30-6:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
February 19, 2004

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Claims 1-5, 6, 8-10 are pending.

Response to Amendment

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Allowable Subject Matter

2. Claims 1, 5, 6, 8-10 define over the prior art of record and are allowed.

New Grounds of Rejection

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 3-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. .

The test kit of claims 3 and 4 are directed to the combination of three affinity reagents for the determination of a protein macromolecule, wherein the affinity reagent is a lectin, cofactor, receptor or nucleic acid.

Lectins bind to carbohydrates by definition and would not serve as an affinity reagent to detect a protein macromolecule. The claimed test kits that comprise three lectins, wherein the

macromolecule is a protein, is not enabled for the detection of a protein macromolecule in a sample as lectins are not protein affinity reagents.

Cofactors are atoms or molecules specific for a different molecule and include zinc, copper, iron, heme, Fe-S, Mn, Mg, ATP, GTP, NAD to name a few. No combination of three affinity Cofactors for a single protein that would evidence binding sites in proximity to one another have been described in the instant specification. Any combination of three affinity Cofactors would not predictably bind to any protein macromolecule especially when the protein does not utilize a cofactor, or only has affinity for a single cofactor, not three. The instant specification has not enabled test kits that comprise three Cofactors that evidence affinity and simultaneously bind to the claimed genus of protein macromolecules, wherein the second and third Cofactors bind to different epitopes that are in proximity to one another to permit amplification or ligation of the oligonucleotide labels attached to the Cofactors. The instant specification has not provided guidance, nor teaches how any three Cofactors could be used to detect any protein macromolecule in a sample. The test kits that comprise three affinity reagents that are Cofactors are not enabled as they do not evidence the required functional limitations recited in the claims. No examples have been provided to define or show the missing information. The person of skill in the art would be required to perform undue experimentation to identify how any protein macromolecule could be detected using any combination of Cofactors, especially when the protein does not evidence natural binding characteristics for three different Cofactors, or have binding site sufficiently close to one another to permit the detection/amplification/ligation of

the oligonucleotides conjugated to the three Cofactors. Kits that comprise three affinity Cofactors are not enabled for the detecting the recited genus of protein macromolecules.

Additionally the instant specification has not enabled the utilization of three receptors to simultaneously bind to a single protein macromolecule to detect the macromolecule in a sample. The instant specification has not described any protein macromolecules that would bind to three affinity receptors simultaneously, with epitopes sufficiently close to each other to permit the oligonucleotides conjugated to the second and third receptors to be ligated or amplified. Stearic hindrance would also serve to prevent affinity binding between the second and third receptors, as well as prevent amplification or ligation of the oligonucleotide labels attached to the receptors. The receptors recited in the claims are not limited to protein receptors, and carbohydrate, lipid and nucleic acid receptors are known in the art so any combination of three receptors would not serve as affinity reagents to simultaneously bind to and detect a single protein macromolecule. The claimed kits are not enabled for the detection of protein macromolecule using three receptors. The person of skill in the art would de novo, be required to identify, what combination of three receptors would function as affinity reagents to detect a single macromolecule, as the instant specification has not described any combinations of receptors that would serve as affinity reagents with the recited abilities to bind in such close proximity. The instantly claimed kits that comprise three receptors is not enabled.

The instant specification also has not described, nor enabled the utilization of three nucleic acids to simultaneously bind to and detect a single protein macromolecule in a sample,

wherein the protein macromolecule would bind to three different affinity reagent nucleic acids simultaneously, with epitopes/binding sites for the second and third nucleic acid affinity reagents sufficiently close to each other to permit the oligonucleotide conjugated thereto to be ligated or amplified. Nucleic acids are known in the art to bind to other nucleic acids and not to any protein macromolecule; any combination of nucleic acids would not serve as affinity reagents to simultaneously bind to and detect a protein macromolecule through amplification and ligation of the conjugate oligonucleotide labels attached thereto. The claimed kits are not enabled.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 2 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 4 (claim 4 is dependent from claim 2) define the "macromolecule" to be " a specific antigen" and depends from claim 1 which defines the "macromolecule is a protein". Claim 2 broadens the scope of claim 1, as all antigens are not proteins. Antigens are known to include carbohydrates, oxidized nucleic acids, lipopolysaccharides. This rejection could be obviated by amending the claims to recite --protein antigen--.

Claim 3 and 4 recites affinity reagents that are "lectins, receptors, Cofactors or nucleic acids"; Claim 3 broadens the scope of claim 1 from which it depends because:

a. lectins to do not bind to protein macromolecules, but to carbohydrates;

b. the receptors are not defined to be protein macromolecule receptors;and

c. the nucleic acids bind to nucleic acids not proteins.

7.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
July 11, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600